Amendments to the Specification:

Please replace the paragraph beginning at page 7, line 17 with the following amended paragraph:

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) J. Mol. Biol. 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package ~~(available at http://www.gcg.com)~~, using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package ~~(available at http://www.gcg.com)~~, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. Another set of parameters (e.g., that can be used if the practitioner is uncertain about what parameters should be applied to determine if a molecule is within a sequence identity or homology limitation of the invention) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

Please replace the paragraph beginning at page 8, line 1 with the following amended paragraph:

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences (such as human ΔTRα1, ΔTRα2, or myosin V amino acid or nucleic acid sequences). Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to nucleic acid molecules useful in the invention (such as

human ΔTRα1, ΔTRα2, or myosin V). BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules useful in the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. ~~See http://www.ncbi.nlm.nih.gov.~~

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Canceled)

2. (Currently amended) The method of claim [[1]] 50, wherein the ligand is a flavone.

3. (Currently amended) The method of claim [[1]] 50, wherein the ligand is an aurone.

4. (Currently amended) The method of claim [[1]] 50, wherein the ligand is a T4 analog.

5-49. (Canceled)

50. (New) A method of assaying a translation product of a mutant ΔTRα2 gene, the method comprising

(a) providing a test cell that comprises p29 vesicles and a mutant ΔTRα2 translation product;

(b) contacting the test cell with a labeled ΔTRα2 ligand for a time sufficient to permit binding to the translation product; and

(c) measuring the amount, location, or rate of transit of the ligand in the test cell compared to the amount, location, or rate of transit of the ligand in a control cell that does not comprise a mutant ΔTRα2 translation product.

51. (New) The method of claim 50, wherein the cell is a neuron.

52. (New) The method of claim 50, wherein the cell is an astrocyte.

53. (New) The method of claim 50, wherein the amount of the ligand in the cell is measured.

54. (New) The method of claim 50, wherein the location of the ligand in the cell is measured.

55. (New) The method of claim 50, wherein the rate of transit of the ligand in the cell is measured.

56. (New) The method of claim 50, wherein the control cell comprises a wild type ΔTRα2 protein, and a decrease in the amount location, or rate of transit of the ligand in the test cell compared to the control indicates a decrease in the ability of the translation product to transport a vesicle compared to a wild type ΔTRα2 protein.

REMARKS

Claims 2-4 and 50-56 are pending. Claims 50-56 are newly added, and claims 1 and 5-49 are cancelled by the present amendment. Claims 2-4 are amended to alter their dependencies. Claim 50 effectively replaces claim 1 as the sole independent claim. Claim amendments are supported throughout the specification, e.g., at page 2, lines 20-28 and page 19, line 30-page 20, line 8. No new matter is added by the amendments.

Specification

The specification has been objected to because is contains browser-executable code. Applicants have deleted the browser executable code. Accordingly, applicants request that the rejection be withdrawn.

35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-4 have been rejected for an alleged lack of enablement. The Office Action asserts that the specification is "enabling for the claimed method wherein the recited 'functionality' is limited to thyroid hormone-mediated vesicle transport" (Office Action at page 2).

Applicants have replaced claim 1 with new claim 50, which does not use the term "functionality" and expressly states that the amount, location, or rate of transit of a mutant ΔTRα2 translation product is assayed and compared to a control cell. Applicants believe that this is within the scope of the material that the Office Action finds enabled.

The Office Action also states "the cell in which the assay is performed is limited to a neuronal cell, does not reasonably provide enablement for the method as broadly claimed" (Office Action at pages 2-3), and "neither the art nor the specification discloses ... any other cells [besides neuronal cells] in which ΔTRα2 is active (Office Action at page 3, second full paragraph). Applicants respectfully disagree with this conclusion.

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8USPQ2d 1217, 1223 (Fed. Cir. 1988).

Applicants believe that the claims are enabled for a broader scope of cells than only neuronal cells. Claim 50 recites a cell that comprises p29 vesicles and a mutant ΔTRα2 translation product. It is clear from the specification that the claimed invention can be carried out using cells that contain p29 vesicles (e.g., specification at pages 32-38). One in the art would readily know how to identify such a cell. In addition, the specification describes ΔTRα2 activity not only in neurons, but also in glia (e.g., astrocytes, for example see pages 32-38 of the specification), a non-neuronal cell type that contains p29 vesicles.

In view of the above, applicants believe that one in the art would be able to carry out the claimed invention using cell types other than neuronal cells and respectfully request that the rejection under 35 U.S.C. § 112, be withdrawn.

CONCLUSION

In view of the claim amendment and the arguments presented above, applicants believe that the claims are in condition for allowance, which action is requested.

Enclosed is a $465 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket number 07917-103001.

Respectfully submitted,

Date: September 25, 2003

Lisa N. Geller, Ph.D., J.D.
Reg. No. 51,726

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

20729430.doc